Molecular Crystals and Liquid Crystals Incorporating Nonlinear Optics

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A STUDY OF THE MECHANISM OF HYDROLYSIS OF SINGLE CRYSTALS OF 2-PHENYL-4H-3,1-BENZOXAZIN-4-ONE

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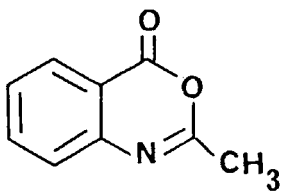
Abstract Single crystals of 2-phenyl-4H-3,1-benzoxazin-4-one, **1**, (*a* = 13.315 Å, *b* = 3.912 Å, *c* = 20.465 Å, β = 94.93°, Z = 4, $P2_1/n$, R = 0.047) have been found to undergo hydrolysis[1] at room temperature. Reacting single crystals were observed to react first at needle ends of crystals with the reaction proceeding along the *b* axis of the needle. The chemical mechanism and the reaction pathway in the solid is rationalized by chemical results (analysis of mass spectra resulting from ^{18}O water experiments) and theoretical calculations based on the X-ray data. Evaluation of occupied and free-space in crystal **1** is obtained by the method of Gavezzotti.

Organic single crystals are useful for the study of reaction mechanisms since molecular conformations and intermolecular contacts can be precisely defined from X-ray crystal structure analyses. During solid-state or solid-gas reactions the progress of reaction can be monitored by observing the reaction direction in relation to the morphology of the crystal and by observing the mode of phase separation of the product. The product phase can cause fracturing, powdering, expansion, or sublimation of the crystal, thereby giving additional information

about the mechanism of reaction and, in particular, about the cooperative motions of groups of molecules. Such mechanistic information is unattainable from studies of reactions in mobile phases. The mechanisms of a variety of solid-gas reactions have been reported paying attention to correlations between the progress of the reacting gas throught the molecular organic crystals and the morphology of the crystals[1-4].

We report here the results of a study of the hydrolysis of single crystals of 2-phenyl-4H-3,1-benzoxazin-4-one, 1, which were found to undergo unitropic hydrolysis at room temperature by a mechanism similar to that reported earlier for hydrolysis of the methyl analog even though the crystal structures of 1 and 2 are distinctly different[4].



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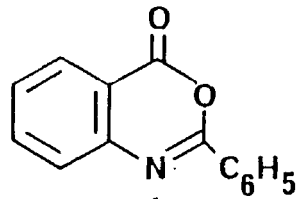

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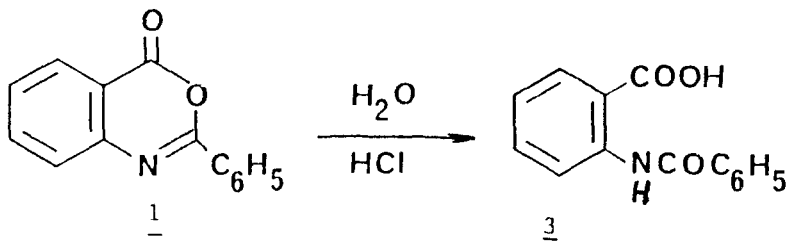
In the present study we correlate the reaction direction, determined from phase front development in the single crystals of 1, with an analysis of the "free-space" available in the crystal, using Gavezzotti's program.

EXPERIMENTAL

Solid-state Reactions

Single acicular crystals of 1[5] were placed in a Petri dish and exposed to air saturated with a 10 % HCl/water vapor, at 25°C, for 1-3 weeks. Reacting single crystals were observed to first react at both needle ends of the crystals, with the reaction proceeding along the axis of the needle. Single crystals did not retain their original morphology. The reaction product grew outside the original crystal faces. We also noticed that higher concentrations of HCl (36 %) caused the reaction to take place faster (3-4 days) with no phase front development. Rather, the crystal faces reacted at the same rates and product formation appeared to occur isotropically. The product, 3, was shown to be pure by tlc and mass spectrometry analysis for both the fast and slow reactions .



1 3

Experiments with air saturated with ^{18}O enriched (98 %) water containing HCl, HCl-H_2O*, followed by mass spectrometry analysis of labelled product 3 showed that the ^{18}O is almost always incorporated in the benzoyl function group. This lead to the conclusion that the hydrolysis is occuring on the imine function[6].

X-ray Structure Analysis

A colorless crystal of 1 (size 0.1x0.2x.03mm) was used for collecting the intensities on an automated four-circle CAD4 diffractometer. Lattice parameters obtained from least-squares analysis of 25 reflections are: a = 13.315(2), b = 3.912(2), c = 20.465(4) Å, β = 94.93°(1). Filtered Mo radiation and the θ-2θ scan techniques were used during collection of 1949 reflections in the range $0 \leq 30°0$. Of these 731 were regarded as observed ($I<3\sigma I$). Three standard reflections showed no crystal decay. The structure was solved by direct methods (MULTAN 80) in the monoclinic $P2_1/n$ space group (Z = 4) and refined by full-matrix least-squares procedure to R = 0.047 for 720 F obs. The function minimized was $\sum_i \omega_i(F_o - F_c)2$, where $\omega = 4F_o^2/\sigma F_o^2$ and was taken from counting statistics, Rw = 0.048. Hydrogen atoms were included in structure factor calculations at their calculated positions and held invariant together with isotropic temperature factors set as 4.0 A^2. Final ω = 1.265 and average shift/error ≤0.05. Intensities were corrected by LP and extinction factors but not for absorption μ(MoK) = 0.833 cm^{-1}. Atomic scattering factors were taken from the SDP system which was the basic set of programs for crystallographic calculations. Final atomic coordinates and Beq are shown in Table I *.

As shown in Figure 1, the molecule 1 is almost flat - the angle between least-squares planes of the phenyl and fused hetero-ring systems is only 4°. Weak intermolecular

* Tables of structure factors and anisotropic thermal parameters may be obtained upon request.

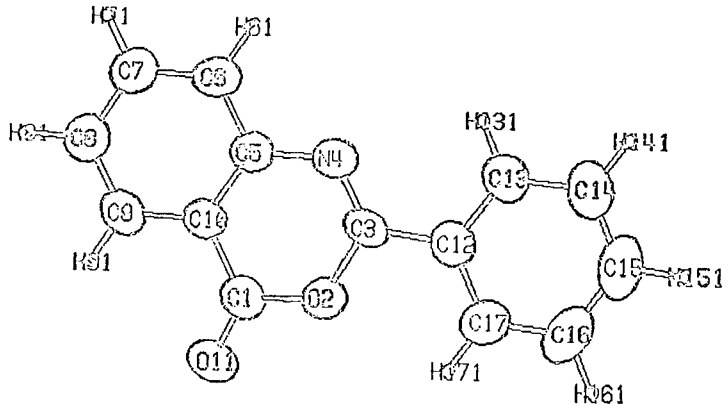


FIGURE 1. Isolated molecule 1.

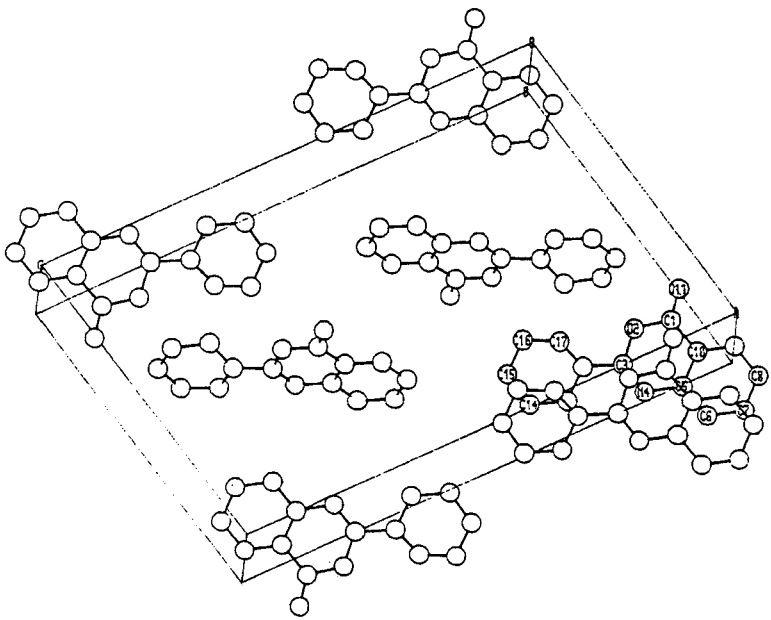


FIGURE 2. Molecular packing in crystal 1.

hydrogen bond of C-H...O type is observed between O2 and H171 with H...O distance 2.376 Å and angle at the H-atom 98.1°. The perspective drawing, Figure 2, shows the crystal lattice consists of layers of centrosymmetric dimers parallel to ac plane. The layers contain carbonyl groups and ring-oxygen atoms, alternatively hydrophobic phenyl rings or hydrophilic N-atoms on the other, parallel to (101).

Free-space Calculation

Gavezzotti's program[7] is designed to take unit cell, atomic parameters and space group information about a crystal and calculate, using rigid sphere approximations for atoms, where "free-space" and "filled-space" regions are in the crystal. Such calculations are useful for defining crystal channels, pockets, or planes of free space. The chemical nature of the surfaces of the space can be determined by comparing the calculated regions of free space with the actual packing patterns of the molecules. We were interested in testing whether "free-space" regions occurred in crystallographic planes corresponding to the direction of motion of the hydrolysis reaction of 1 and to determine whether these regions are sites of reaction, pockets for product segregation, or regions where reactant molecules can expand to transition states for hydrolysis.

The results of the calculations for 1, are shown in Figure 3. Maps of the filled- and free-space regions are shown in crystal planes parallel to (001). Since previous work with isotopically labelled water had shown that hydrolysis occurs only at nitrogen sites, we have shown those planes which contain the nitrogen atoms in the crystal. One can clearly see channels parallel to (100),

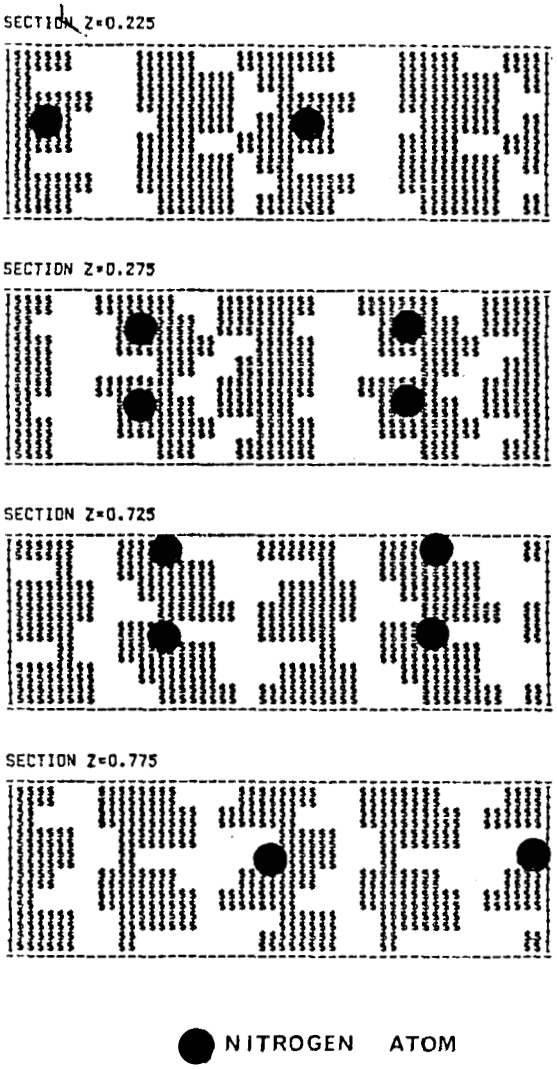


FIGURE 3. Di maps for sections perpendicular to z = 0.225 , 0.275 , 0.725 and 0.775

extending through each layer of the structure. The actual dimensions of the channel are variable, with the widest dimension equal to about 3 Å.

DISCUSSION

Comparison of the crystal packing pattern with the maps of "free-space" regions shows that the nitrogen atoms, which are the hydrolysis sites, are located on the surfaces of the void spaces. The void channels are parallel to the b-axis consistent with the observation of reaction frontal motion along b, the needle axis of the crystal. These results suggest that the motion of water and HCl molecules along these channels is assisted by the formation of hydrogen-bonds to the nitrogen atoms.

Since 1 does not react at any appreciable rate with water, we used acidic water vapor to promote reaction and found that reaction rates were increased with increase in concentration of acid. We do not know the exact role of acid in the solid-state reaction, but acid catalysis is needed in order to effect hydrolysis of 1 in solution as well. In the solid state HCl could also hydrogen bond to the nitrogen atoms in the void cavities. Clearly, if water with a short dimension of 1.40 Å and HCl with its shortest dimension equal to 1.80 Å, were to move through the lattice of 1 by forming hydrogen bonds to nitrogen, considerable strain would develop in the crystal and expansion, fracturing, or complete crystal disintegration would be expected. We observe the reactant crystal becoming opaque (the opacity defines the position of the

reaction front) due to formation of microcrystallites as reaction takes place. Analysis of the opaque regions shows that they are composed only of product. Thus, product formation could be causing the breakdown of the reactant crystal. It is also possible, however, that the opacity develops as water (and HCl) hydrogen bonds to molecules of 1 due to formation of a disordered lattice. We have found that increased reaction rates occur when the concentration of HCl is increased, consistent with this mechanism. In this case, product formation would be promoted by the increased mobility of molecules in a disordered lattice, and by the presence of intimately associated molecules of 1 and water.

The observation that the product phase actually grows outside the original reactant crystal faces is indicative of solid-state recrystallization of the product occurring following reaction. With water vapor as well as water of hydration present in the crystal, there may be sufficient motion in the solid state, and in regions of the disordered lattice which actually contain liquid water, to allow long range molecular motions and the growth of nucleation sites beyond the confines of the original lattice.

CONCLUSION

The solid-state hydrolysis of 1, promoted by the presence of HCl, involves at least three independent reaction steps. First, water (and HCl) penetrates the lattice along channels of free space in the crystal. The motion of the water is assisted by formation of hydrogen bonds to nitrogen atoms of 1 which line the interior of the void

space. The void space is not large enough to accomodate the hydrated species so the motion of water is accompanied by crystal lattice degradation and the presence of a phase front. We believe that this step is the rate determining step. The second step is most likely product formation which occurs in the disordered reactant lattice at sites containing the hydrogen-bonded form of 1. The third step would be product segregation which is promoted by the presence of water in the solid state and by water vapor in crystal defect sites, allowing long range motion of the product molecules and the formation of product crystallites outside of the faces of the original reactant crystal.

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